

### **REMARKS**

These remarks are in response to the Final Office Action mailed May 3, 2005. Claims 1, 9-13, 15, 22-23, 26 and 32 have been amended. Claims 2-8 and 17-21 have been canceled without prejudice. Claims 14 and 33 were previously canceled and withdrawn, respectively. Support for the amendments can be found throughout the specification and claims as filed. Hence, claims 1, 9-13, 15-16 and 22-32 are pending.

Accordingly, no new matter has been added and entry of the amendment is respectfully requested.

#### **I. Amendment to the Claims**

Claims 1, 9-13, 15, 22-23, 26 and 32 have been amended.

The claims have been amended to recite "an enriched population of cells" and a method of making "an enriched population of cells" which are not teratogenic in SCID mice and express a first and a second polypeptide or mRNA marker from at least two different cell types, wherein the cell types are selected from ectodermal cells, mesodermal, or endodermal cells, and wherein the first marker is selected from the group consisting of nestin, vimentin, neurofilament light isoform, microtubule-associated protein 2c, tau, nonphosphorylated neurofilament heavy isoform, neuron-specific enolase, tyrosine hydroxylase, glial fibrillary acidic protein, CNPase, and galactocerebroside, and the second marker is selected from the group consisting of myf-6, myosin light-chain 2 ventricular isoform, flk1,  $\alpha$ -1-fetoprotein and GATA-4.

Claims 2-8 and 17-21 have been canceled because their subject matter has been incorporated into the amended claims above.

The above amendments are fully supported in the specification as filed and no new matter has been added.

**II. Rejection Under 35 U.S.C. §112, second paragraph (indefiniteness)**

Claims 22-31 are rejected under 35 U.S.C. § 112, second paragraph for allegedly failing to point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse this rejection on the following grounds.

According to the Office, the phrase, “reduced serum” is not defined in the specification and does not have clear meaning in the art.

However, Applicants submit that “reduced serum” is described in the art. For example, on page 57, paragraph [0163], reduced serum is described as “5%.” This definition is also confirmed on page 46, paragraph [0134], where Applicants have provided at least two examples of “reduced serum” media: “EGM2mv (Clonetics), various muscle-specific growth media and hepatocyte maintenance media (Hepatostim, Collaborative BioAlliance, Stony Brook, NY).” Exhibit A (Clonetics™ Endothelial Media Systems; 1 page product sheet and 2 pages from the online version of the Product Catalog) shows that EGM-2-MV has a final serum content increased to 5%. Hence, Applicants submit that the phrase, “reduced serum,” is sufficiently described such that one skilled in art is apprised of the serum content of the cell culture media.

Accordingly, withdrawal of the rejection of claims 22-31 under 35 U.S.C. § 112, second paragraph, is respectfully requested.

**III. Rejections Under 35 U.S.C. §102(b)**

All claims are variously rejected under 35 U.S.C. § 102(b) as being allegedly unpatentable because they are anticipated by Allsopp et al. (1995; hereinafter, “Allsopp”), Jin et al. (1993; hereinafter, “Jin”), Li et al. (1996; hereinafter, “Li”), Damjanov et al. (1993; hereinafter, “Damjanov”) and Lefebvre et al. (1998; hereinafter, “Lefebvre”). Applicants respectfully traverse all these rejections.

Under 35 U.S.C. § 102, “[a] claim is anticipated only if *each and every element* as set forth in the claim is found, either expressly or inherently described, in a single prior art reference

(emphasis added).” *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 0987). Further, “[t]he identical invention [should it be taught in the cited reference] must be shown in as complete detail as is contained in the ...claim.” *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Applicants submit that in view of the following remarks, none of the cited references anticipates the claimed invention, because each reference does not teach *each and every element* of the claimed invention.

A. Claims 1-5, 9-13, 15, 16 and 18-20 stand rejected under 35 USC §102(b), as allegedly being anticipated by Allsopp. Applicants respectfully traverse this rejection.

Claims 2-5 and 18-20 have been canceled, thus making rejections to these claims moot. Thus, Applicants address the rejection with regards to pending claims 1, 9-13 and 15-16.

According to the Office Action, Allsopp discloses a cell containing markers (e.g., nestin) characteristic of at least two different cell types.

Applicants submit that after a detailed review of Allsopp, Applicants were unable to determine where Allsopp discloses nestin “as evidenced by Jiang (see page 3 of the Office Action).” That is, Applicants were unable to identify the “Jiang” reference in the text or in the references cited in the document. Thus, clarification of this is respectfully requested.

However, to be fully responsive and advance the prosecution of the above-identified application, Applicants submit that even if Allsopp does disclose expression of a nestin, Allsopp does not disclose that “a first and a second polypeptide or mRNA marker from two different cell types.” Allsopp discloses a first marker, but Allsopp does not disclose a second marker (e.g., wherein the second marker is selected from the group consisting of myf-6, myosin light-chain 2 ventricular isoform, flk1,  $\alpha$ -1-fetoprotein and GATA-4). Therefore, Allsopp cannot anticipate

the claimed invention because it does not disclose each and every element of the claimed invention.

Accordingly, withdrawal of the rejection of pending claims 1, 9-13 and 15-16, under 35 U.S.C. §102(b) is respectfully requested.

B. Claims 1, 6 and 8 stand rejected under 35 USC §102(b), as allegedly being anticipated by Jin. Applicants respectfully traverse this rejection.

Claims 6 and 8 have been canceled, thus making rejections to these claims moot. Thus, Applicants address the rejection with regards to pending claim 1.

According to the Office Action, Jin discloses clonal myoblasts expressing myf6. Also, according to the Office Action, although Jin does teach the expression of nestin, myoblasts inherently express nestin.

Jin does not disclose whether the myoblasts have teratogenic properties in SCID mouse. Therefore, Jin cannot anticipate the claimed invention because Jin does not disclose each and every element of the claimed invention.

Accordingly, withdrawal of the rejection of claims 1-6 and 8 under 35 U.S.C. §102(b) is respectfully requested.

C. Claims 1 and 7 are newly rejected under 35 USC §102(b), as allegedly being anticipated by Li. Applicants respectfully traverse this rejection.

Claim 7 has been canceled, thus making the rejection as to this claim moot. Thus, Applicants address the rejection with regards to pending claim 1.

According to the Office Action, Li discloses human adult and fetal cardiomyocytes, both of which express GATA-4. Further, according to the Office Action, because GATA-4 is a marker of cardiac muscle and gastrointestinal tissues, it allegedly meets the limitation that cells express markers from two different cell types.

Applicants submit that the claimed invention recites a cell having a first and a second marker from at least two different cell types (see claim 1). Hence, although GATA-4 is disclosed in Li, GATA-4 is a second marker, and Li does not disclose a first marker as recited in the claimed invention. Therefore, Li does not anticipate the claimed invention because Li does not disclose each and every element of the claimed invention.

Accordingly, withdrawal of the rejection of claim 1 under 35 U.S.C. §102(b) is respectfully requested.

D. Claims 17, 19 and 21 stand rejected under 35 USC §102(b), as allegedly being anticipated by Damjanov. Applicants respectfully traverse this rejection.

Claims 17, 19 and 21 have been canceled, thus making rejections to these claims moot.

Accordingly, withdrawal of the rejection of claims 17, 19 and 21 under 35 U.S.C. §102(b) is respectfully requested.

E. Claims 1, 11-13 and 15-19 stand rejected under 35 USC §102(b), as allegedly being anticipated by Lefebvre. Applicants respectfully traverse this rejection.

Claims 17-19 have been canceled, thus making rejections to these claims moot. Thus, Applicants address the rejection with regards to pending claims 1, 11-13 and 15-16.

According to the Office Action, Lefebvre discloses human pancreatic islet cells, which express markers from two different cell types.

However, Lefebvre does not disclose a first *and* a second marker from two different cell types. Thus, absent this showing Lefebvre is not prior art with respect to the claimed invention. Further, even if Lefebvre inherently discloses nestin, nestin alone is only a first marker of the claimed invention. Lefebvre would still have to show a second marker as recited in claim 1 in order to anticipate the claimed invention.

Accordingly, the withdrawal of the rejection of claims 1, 11-13 and 15-16 under 35U.S.C. §102(b) is respectfully requested.

#### **IV. Rejection Under 35 U.S.C. §103(a)**

Claims 21-32 are rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Shamblott (1998) in view of Yuen (1998).

Claim 21 has been cancelled, thus making the rejection to claim 21 moot. Thus, Applicants address the rejection with regards to pending claims 22-32.

According to the Office Action, Shamblott discloses cystic embryoid bodies which express markers of at least two different cell types. Yuen discloses cell culture conditions not permissive for EG cells and culture media lacking LIF and a fibroblast feeder layer. Thus, according to the Office Action, Shamblott in view of Yuen teach or make obvious all of the claim limitations.

However, Shamblott does not disclose both a first and a second marker as in the claimed invention. Shamblott discloses cells reactive to  $\alpha$ -1-fetoprotein, an endodermal marker. Shamblott does not disclose that the cells derived from the embryoid bodies will proliferate in

reduced serum or serum free media. In contrast, the cells in Shamblott require 15% FBS (page 13727, col. 1, first paragraph).

Yuen does not disclose that which is lacking in Shamblott because Yuen discloses cells which proliferate in 10% FCS. As discussed above, "reduced serum" as recited in the claims is supported in the specification as filed and is also understood by those skilled in the art (see Exhibit A which is described in the specification as filed and which shows further defines "reduced serum" as having no greater than 5% serum).

Thus, Shamblott in view of Yuen do not disclose methods of making a population of cells as in the claimed invention, nor do they render such methods obvious.

Accordingly, the withdrawal of claims 1, 11-13 and 15-16 under 35 U.S.C. § 103(a) is respectfully requested.

In re Application of:  
Shamblott, et al.  
Application No.: 09/767,421  
Filed: January 22, 2001  
Page 14

PATENT  
Attorney Docket No.: JHU1750-1

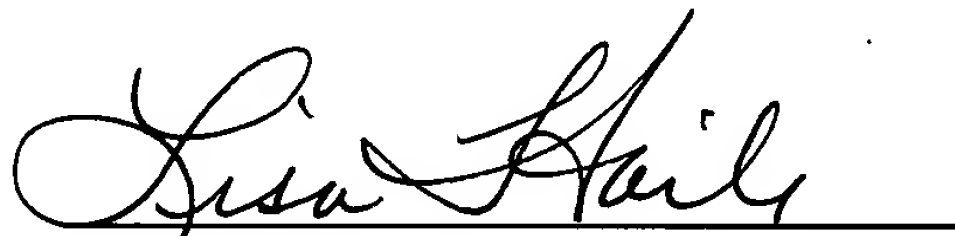
### CONCLUSION

Applicants submit that the pending claims are in condition for allowance. Reexamination, reconsideration, withdrawal of the rejections, and early indication of allowance are requested respectfully. If any questions remain, the Examiner is urged to contact the undersigned below.

No fee is believed due in connection with this Amendment. A check in the amount of \$790.00 is enclosed as payment for the Request for Continued Examination fee. If any additional fees are due, the Commissioner is hereby authorized to charge any additional fees or credit any overpayments to Deposit Account No. 07-1896. A duplicate copy of the Transmittal Sheet is attached.

Respectfully submitted,

Date: October 17, 2005



Lisa A. Haile, J.D., Ph.D.

Registration No. 38,347

Telephone: (858) 677-1456

Facsimile: (858) 677-1465

DLA PIPER RUDNICK GRAY CARY US LLP  
4365 Executive Drive, Suite 1100  
San Diego, California 92121-2133  
**USPTO Customer Number 28213**



# Clonetics™ Endothelial Media Systems

## Product Information



### Endothelial Media Differences

#### EGM® Endothelial Growth Media & EGM BulletKit®

- Basal media developed for normal human endothelial cells in a low-serum environment
- EGM includes an attached aliquot of Bovine Brain Extract (BBE)
- EGM BulletKit includes all supplements and growth factors in separate, frozen aliquots
- Final serum concentration 2%

#### EGM-MV BulletKit

- Developed for microvascular and coronary artery endothelial cells
- Basal medium is unchanged
- Final serum concentration increased to 5%

#### EGM-2 BulletKit

- Refinements to basal medium and the growth factors
- Further defined, does not contain BBE
- Final serum concentration 2%

#### EGM-2-MV BulletKit

- Developed for the enhanced growth of lung microvascular cells
- Final serum concentration increased to 5%

#### EGM-2 BulletKit (CC-3162)

- No BBE (Bovine Brain Extract)
- hEGF
- Hydrocortisone
- GA-1000 (Gentamicin, Amphotericin-B)
- FBS 10 ml
- VEGF
- hFGF-B (w/ heparin)
- R<sup>3</sup> -IGF-1
- Ascorbic Acid
- Heparin

#### EGM-2-MV BulletKit (CC-3202)

- No BBE (Bovine Brain Extract)
- hEGF
- Hydrocortisone
- GA-1000 (Gentamicin, Amphotericin-B)
- FBS 25 ml
- VEGF
- hFGF-B (w/ heparin)
- R<sup>3</sup> -IGF-1
- Ascorbic Acid

### SingleQuot® Kit Contents

#### EGM (CC-3024) EGM-BulletKit (CC-3124)

- BBE (Bovine Brain Extract), with heparin
- hEGF
- Hydrocortisone
- GA-1000 (Gentamicin, Amphotericin B)
- FBS 10 ml

#### EGM-MV BulletKit (CC-3125)

- BBE (Bovine Brain Extract), w/ heparin
- hEGF
- Hydrocortisone
- GA-1000 (Gentamicin, Amphotericin B)
- FBS 25 ml

Cambrex Bio Science Walkersville, Inc.

[www.cambrex.com/bioproducts](http://www.cambrex.com/bioproducts)

[biotechserv@cambrex.com](mailto:biotechserv@cambrex.com)

Orders: 800-638-8174 Technical Service: 800-521-0390

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